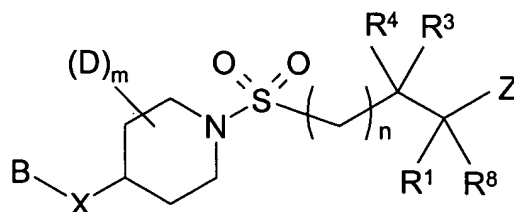


Amendments to the Claims:

This listing of claims replaces all prior versions and listings of claims in the application:

Listing of Claims:

1. (Original) A compound of formula (1):



formula (1)

wherein  $Z$  is selected from  $-\text{CONR}^{15}\text{OH}$  and  $-\text{N}(\text{OH})\text{CHO}$ ;

$R^{15}$  is hydrogen or  $\text{C}_{1-3}$ alkyl;

wherein  $R^1$  is hydrogen or a group selected from  $\text{C}_{1-6}$ alkyl,  $\text{C}_{2-6}$ alkenyl,  $\text{C}_{2-6}$ alkynyl,  $\text{C}_{3-7}$ cycloalkyl,  $\text{C}_{5-7}$ cycloalkenyl, aryl, heteroaryl and heterocyclyl where the group is optionally substituted by one or more substituents independently selected from halo, nitro, cyano, trifluoromethyl, trifluoromethoxy,  $\text{C}_{1-4}$ alkyl,  $\text{C}_{2-4}$ alkenyl,  $\text{C}_{2-4}$ alkynyl,  $\text{C}_{3-6}$ cycloalkyl (optionally substituted by one or more  $R^{17}$ ), aryl (optionally substituted by one or more  $R^{17}$ ), heteroaryl (optionally substituted by one or more  $R^{17}$ ), heterocyclyl,  $\text{C}_{1-4}$ alkoxycarbonyl,  $-\text{OR}^5$ ,  $-\text{SR}^2$ ,  $-\text{SOR}^2$ ,  $-\text{SO}_2\text{R}^2$ ,  $-\text{COR}^2$ ,  $-\text{CO}_2\text{R}^5$ ,  $-\text{CONR}^5\text{R}^6$ ,  $-\text{NR}^{16}\text{COR}^5$ ,  $-\text{SO}_2\text{NR}^5\text{R}^6$  and  $-\text{NR}^{16}\text{SO}_2\text{R}^2$ ;

$R^{16}$  is hydrogen or  $\text{C}_{1-3}$ alkyl;

$R^{17}$  is selected from halo,  $\text{C}_{1-6}$ alkyl,  $\text{C}_{3-6}$ cycloalkyl and  $\text{C}_{1-6}$ alkoxy;

$R^2$  is group selected from  $\text{C}_{1-6}$ alkyl,  $\text{C}_{3-6}$ cycloalkyl,  $\text{C}_{5-7}$ cycloalkenyl, heterocycloalkyl, aryl, heteroaryl, aryl $\text{C}_{1-4}$ alkyl and heteroaryl $\text{C}_{1-4}$ alkyl where the group is optionally substituted by one or more halo;

$R^5$  is hydrogen or a group selected from  $C_{1-6}$ alkyl,  $C_{3-6}$ cycloalkyl,  $C_{5-7}$ cycloalkenyl, heterocycloalkyl, aryl, heteroaryl, aryl $C_{1-4}$ alkyl and heteroaryl $C_{1-4}$ alkyl where the group is optionally substituted by one or more halo;

$R^6$  is hydrogen,  $C_{1-6}$ alkyl or  $C_{3-6}$ cycloalkyl;

or  $R^5$  and  $R^6$  together with the nitrogen to which they are attached form a heterocyclic 4- to 7-membered ring;

wherein  $R^8$  is hydrogen or a group selected from  $C_{1-6}$ alkyl,  $C_{3-7}$ cycloalkyl and heterocyclyl where the group is optionally substituted by one or more substituents independently selected from halo, nitro, cyano, trifluoromethyl, trifluoromethoxy and  $C_{1-4}$ alkyl;

or  $R^1$  and  $R^8$  together form a carbocyclic or saturated heterocyclic 3- to 6-membered ring;

wherein  $R^3$  and  $R^4$  are independently hydrogen,  $C_{1-6}$ alkyl,  $C_{3-6}$ cycloalkyl,  $C_{5-7}$ cycloalkenyl, heterocyclyl, aryl or heteroaryl;

wherein n is 0 or 1;

wherein m is 0 or 1;

wherein D is hydrogen,  $C_{1-4}$ alkyl,  $C_{3-6}$ cycloalkyl or fluoro;

wherein X is  $-(CR^9R^{10})-Q-(CR^{11}R^{12})_u-$  where u is 0 or 1;

Q is O, S, SO or  $SO_2$ ;

$R^9$ ,  $R^{10}$ ,  $R^{11}$  and  $R^{12}$  are independently selected from hydrogen,  $C_{1-4}$ alkyl and  $C_{3-6}$ cycloalkyl;

wherein B is  $C_{2-4}$ alkenyl or  $C_{2-4}$ alkynyl, each being optionally independently substituted by a group selected from  $C_{1-4}$ alkyl,  $C_{3-6}$ cycloalkyl, heterocycloalkyl, aryl, heteroaryl, heterocyclyl whereby the group is optionally substituted by one or more halo, nitro, cyano, trifluoromethyl, trifluoromethoxy,  $-CONHR^{13}$ ,  $-CONHR^{13}R^{14}$ ,  $-SO_2R^{13}$ ,  $-SO_2NHR^{13}$ ,  $-SO_2NR^{13}R^{14}$ ,  $-NHSO_2R^{13}$ ,  $C_{1-4}$ alkyl and  $C_{1-4}$ alkoxy;

$R^{13}$  and  $R^{14}$  are independently hydrogen,  $C_{1-4}$ alkyl or  $C_{3-5}$ cycloalkyl;

or  $R^{13}$  and  $R^{14}$  together with the nitrogen to which they are attached form a heterocyclic 4 to 7-membered ring.

or a pharmaceutically acceptable salt or *in vivo* hydrolysable ester thereof.

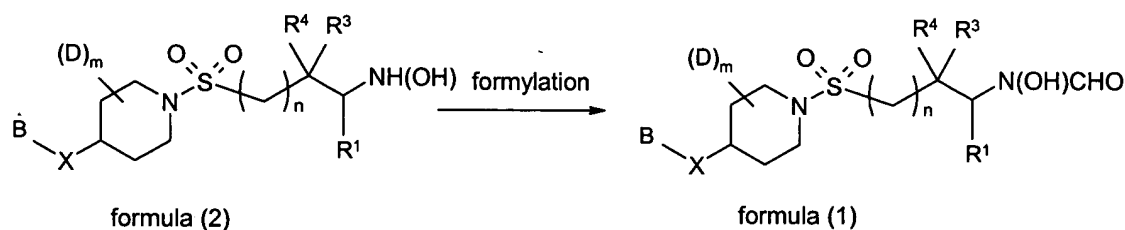
2. (Original) A compound according to claim 1 wherein X is  $-(CH_2)-O-$  or  $-(CH_2)-O-(CH_2)-$ .
3. (Currently amended) A compound according to claim 1 ~~or 2~~ wherein B is  $C_{2-4}$ alkenyl or  $C_{2-4}$ alkynyl, each being optionally independently substituted by  $C_{1-4}$ alkyl,  $C_{3-6}$ cycloalkyl, aryl, heteroaryl or heterocycloalkyl.
4. (Currently amended) A compound according to ~~any one of claims 1 to 3~~ claim 1 wherein  $R^1$  is hydrogen,  $C_{1-6}$ alkyl or aryl where  $C_{1-6}$ alkyl or aryl are optionally substituted by one or more substituents independently selected from  $C_{1-4}$ alkyl, aryl (optionally substituted by  $R^{17}$ ) and heteroaryl (optionally substituted by  $R^{17}$ ) and wherein  $R^{17}$  is halo or  $C_{1-4}$ alkyl.
5. (Cancelled)
6. (Currently amended) A method, the method comprising treating a disease condition mediated by one or more metalloproteinase enzymes by administering to a warm-blooded animal in need of such treatment an effective amount ~~The use of a compound according to any one of claims 1 to 4 claim 1 in the manufacture of a medicament in the treatment of a disease condition mediated by one or more metalloproteinase enzymes.~~
7. (Currently amended) A method, the method comprising treating a disease condition mediated by  $TNF\alpha$  by administering to a warm-blooded animal in need of such treatment an effective amount ~~The use of a compound according to any one of claims 1 to 4 claim 1 in the manufacture of a medicament in the treatment of a disease condition mediated  $TNF\alpha$ .~~
8. (Currently amended) A method of treating autoimmune disease, allergic/atopic diseases, transplant rejection, graft versus host disease, cardiovascular disease, reperfusion injury and

malignancy in a warm-blooded animal, ~~such as man~~, in need of such treatment which comprises administering to said animal an effective amount of a compound according to claim 1.

9. (Currently amended) A pharmaceutical composition comprising a compound according to ~~any one of claims 1 to 4~~ claim 1; and a pharmaceutically-acceptable diluent or carrier.

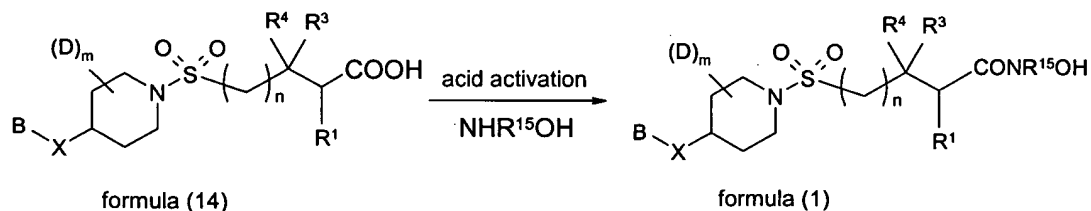
10. (Original) A process for preparing a compound according to claim 1 comprising, when Z is  $-N(OH)CHO$ , the step of:

a) converting a hydroxylamine of formula (2) into a compound of formula (1);



or when Z is  $-CONR^{15}OH$ , the step of:

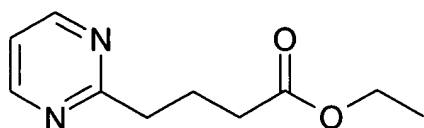
b) converting an acid of formula (14) into a compound of formula (1);



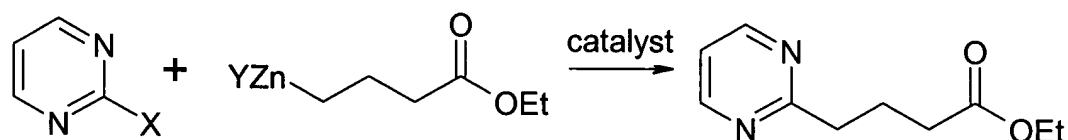
and thereafter if necessary:

- i) converting a compound of formula (1) into another compound of formula (1);
- ii) removing any protecting groups;
- iii) forming a pharmaceutically acceptable salt or *in vivo* hydrolysable ester.

11. (Original) Ethyl 4-(pyrimidin-2-yl)butanoate.



12. (Original) A process comprising the reaction of a 2-halopyrimidine, 2-tosylpyrimidine, 2-pyrimidinyl triflate or 2-pyrimidinyl mesylate with 4-ethoxy-4-oxo-butylzinc bromide or 4-ethoxy-4-oxo-butylzinc iodide in the presence of a catalyst;



wherein X is halo, triflate or mesylate and Y is bromide or iodide.

13. (Original) A process according to claim 11 wherein the catalyst is generated from bis(acetonitrile) palladium (II) dichloride and triphenylphosphine.

14. (Currently amended) A method of effecting a Negishi coupling reaction, the method comprising performing the reaction in the presense of ~~The use of~~ bis(acetonitrile) palladium (II) dichloride and triphenylphosphine ~~in a Negishi coupling reaction.~~